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Combinatorial compound library

- 15,000 compounds screened; collection growing
- Novel "drug like" molecules by Lipinski's "rule of 5"
- Based on 125 templates, 200 congeners each

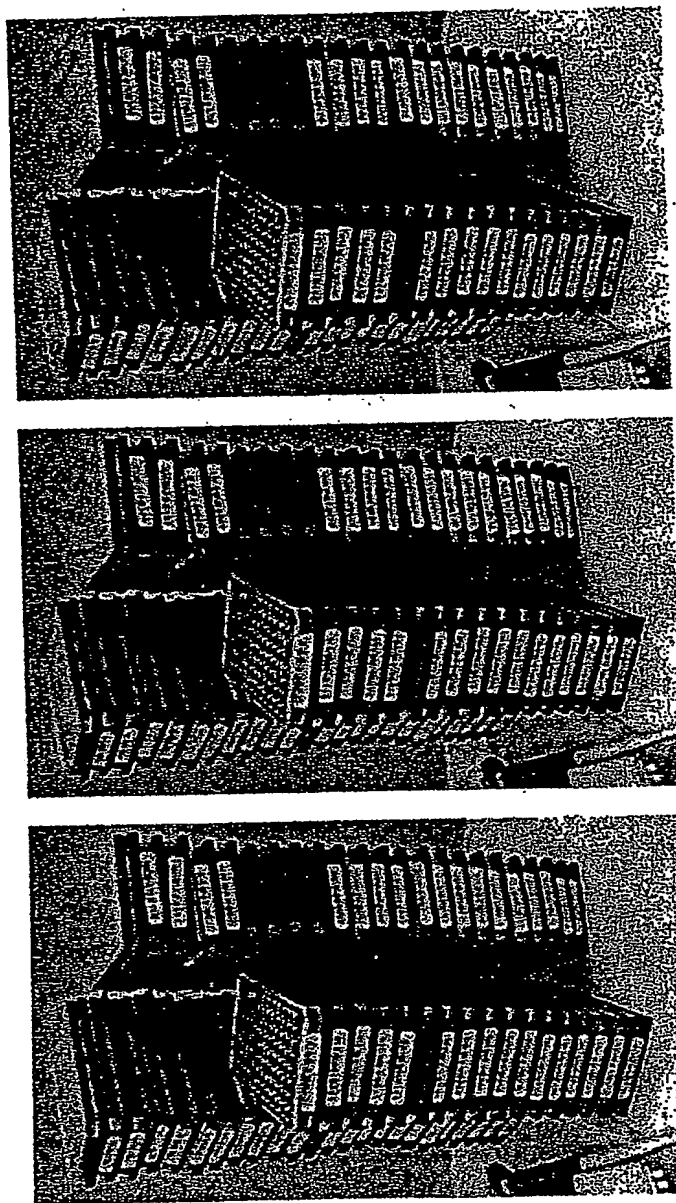
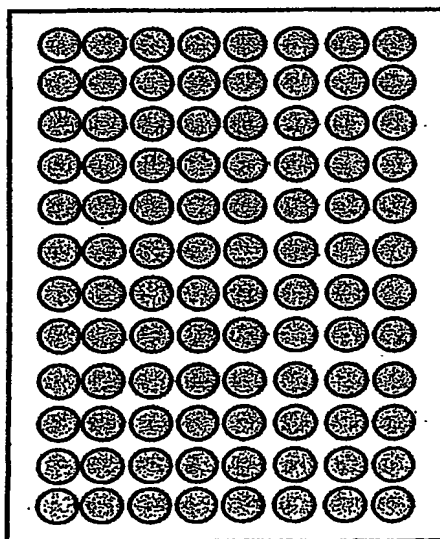


Figure 1

Screening scheme

assay mix/compound/mix



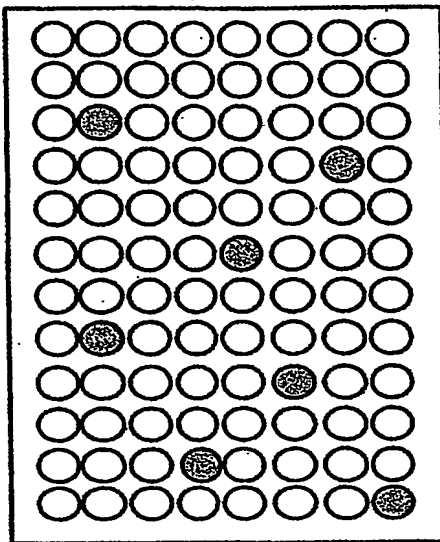
1.5×10^4 neutrophils/well

incubate with test agents

37C for 30 min; add TNF

90 min at 37°C

(T90)

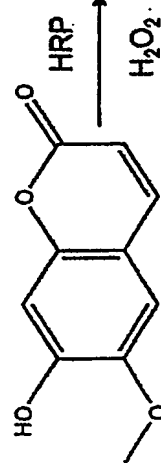


Inhibitors of TNF specific
signaling molecules

Toxicity to neutrophils

Inhibitors of the assay itself (HRP)

Intrinsic fluorescence



6-methoxy 7-hydroxy coumarin

Non-fluorescent

HRP

H_2O_2

Figure 2

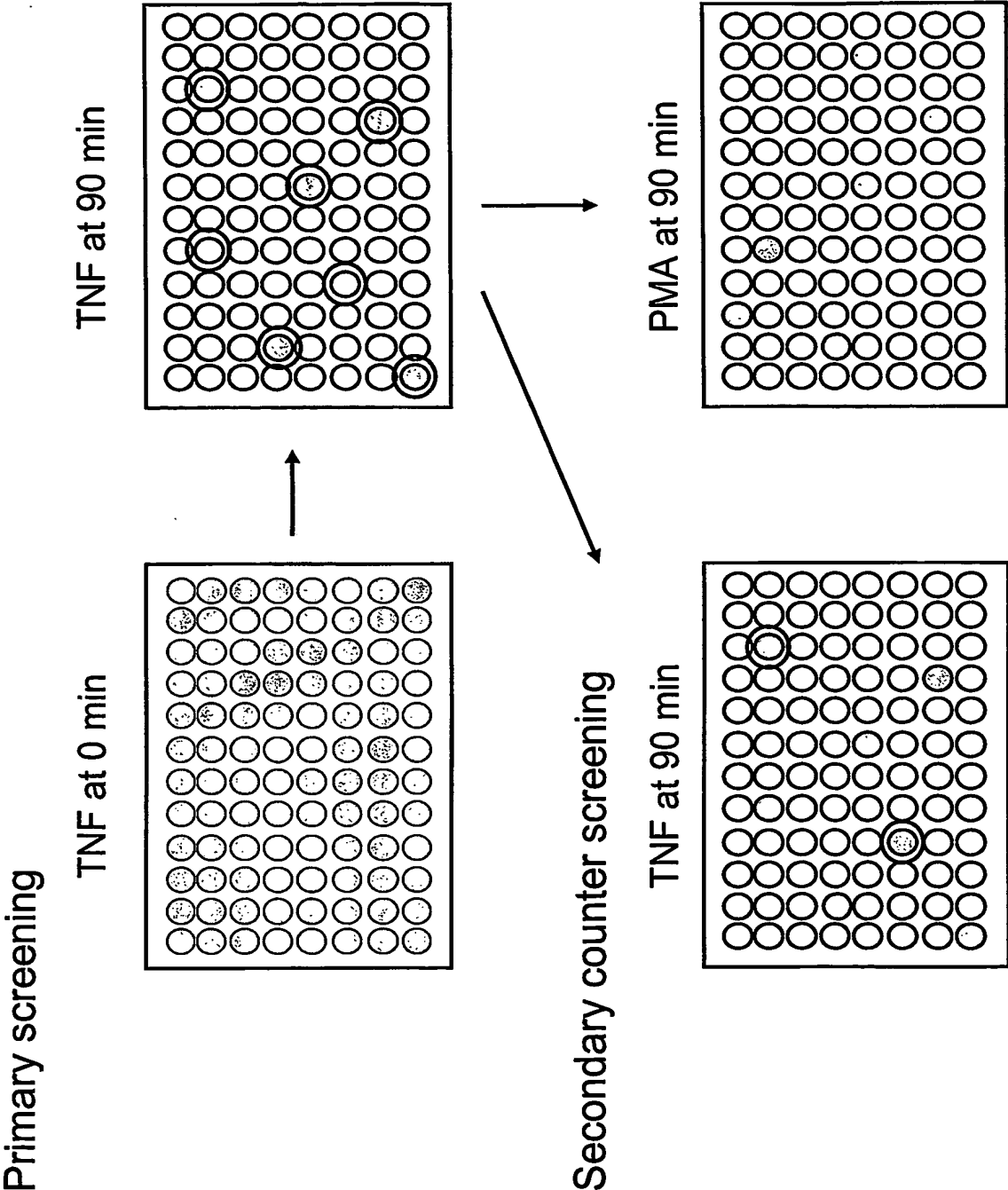


Figure 3

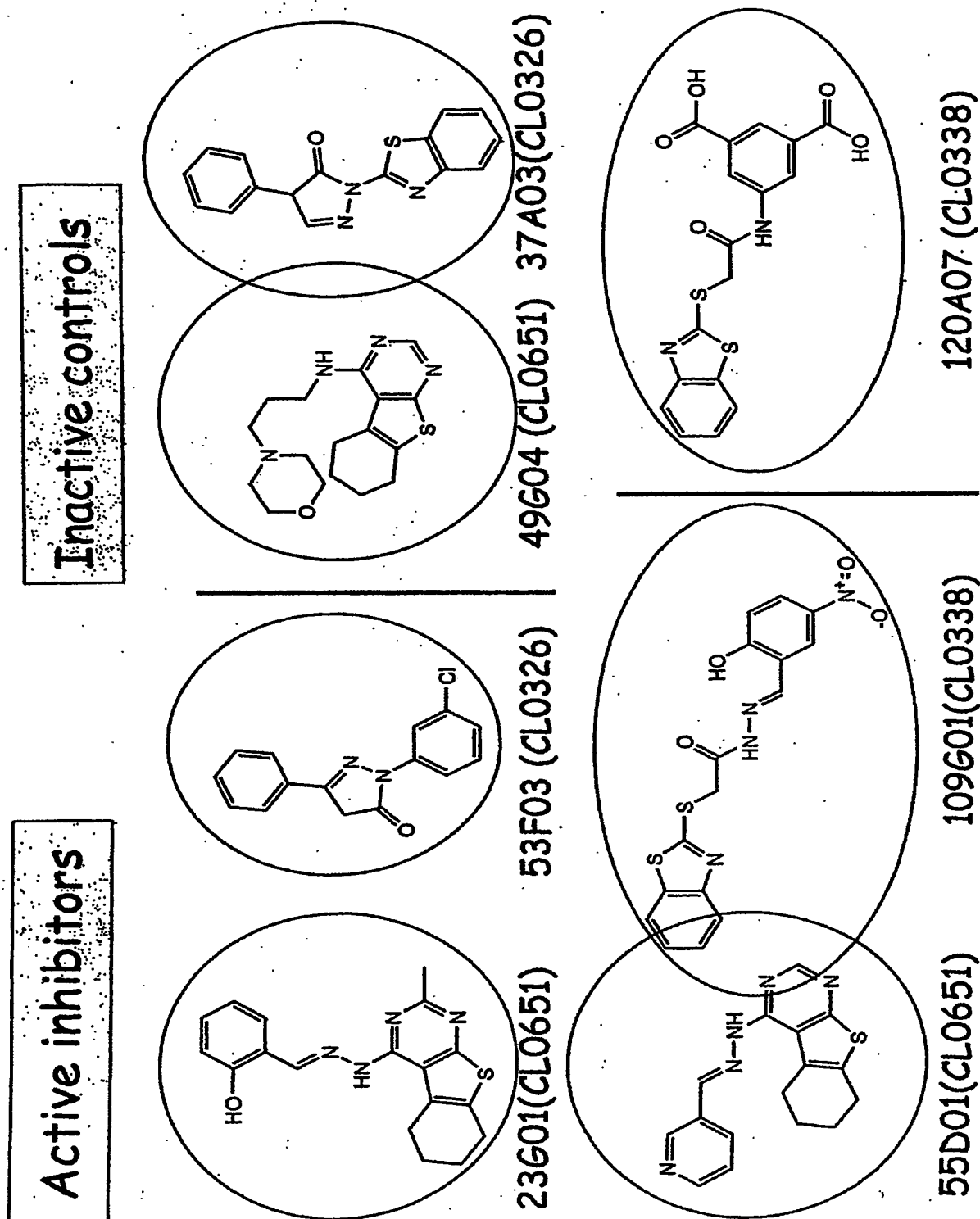


Figure 4

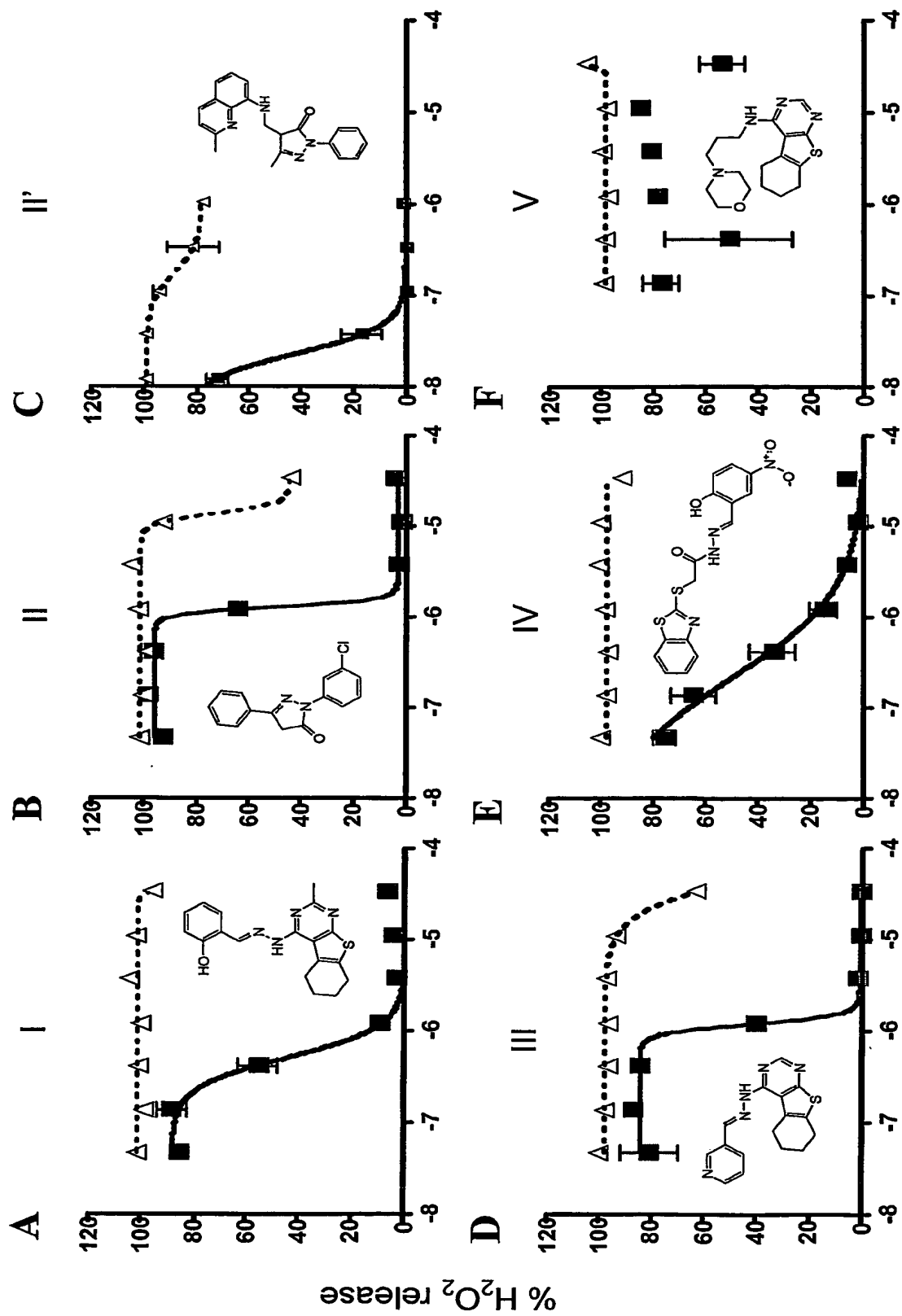
 $\text{Log}_{10} [\text{compound}] \text{ M}$

Figure 5

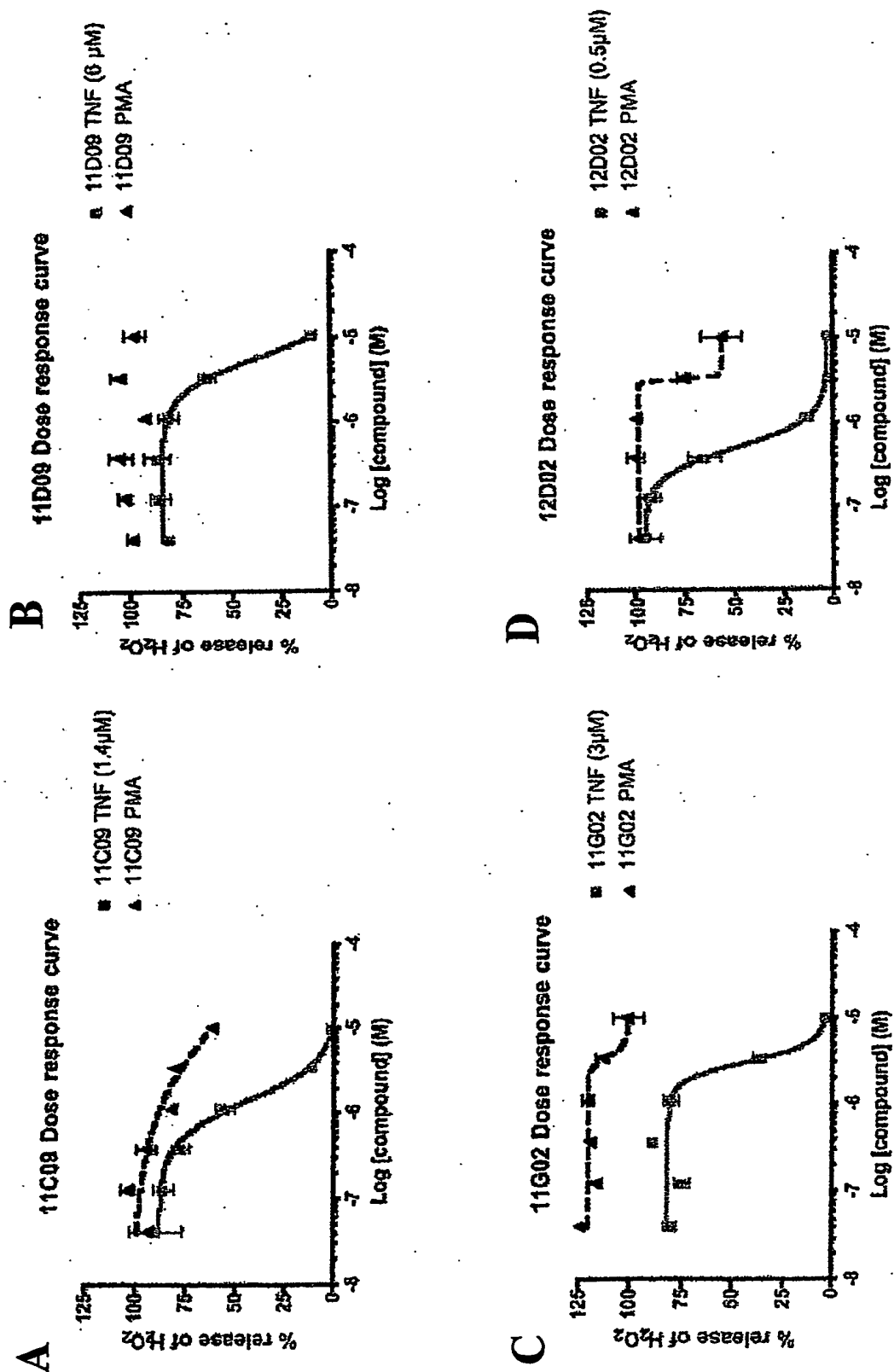


Figure 6

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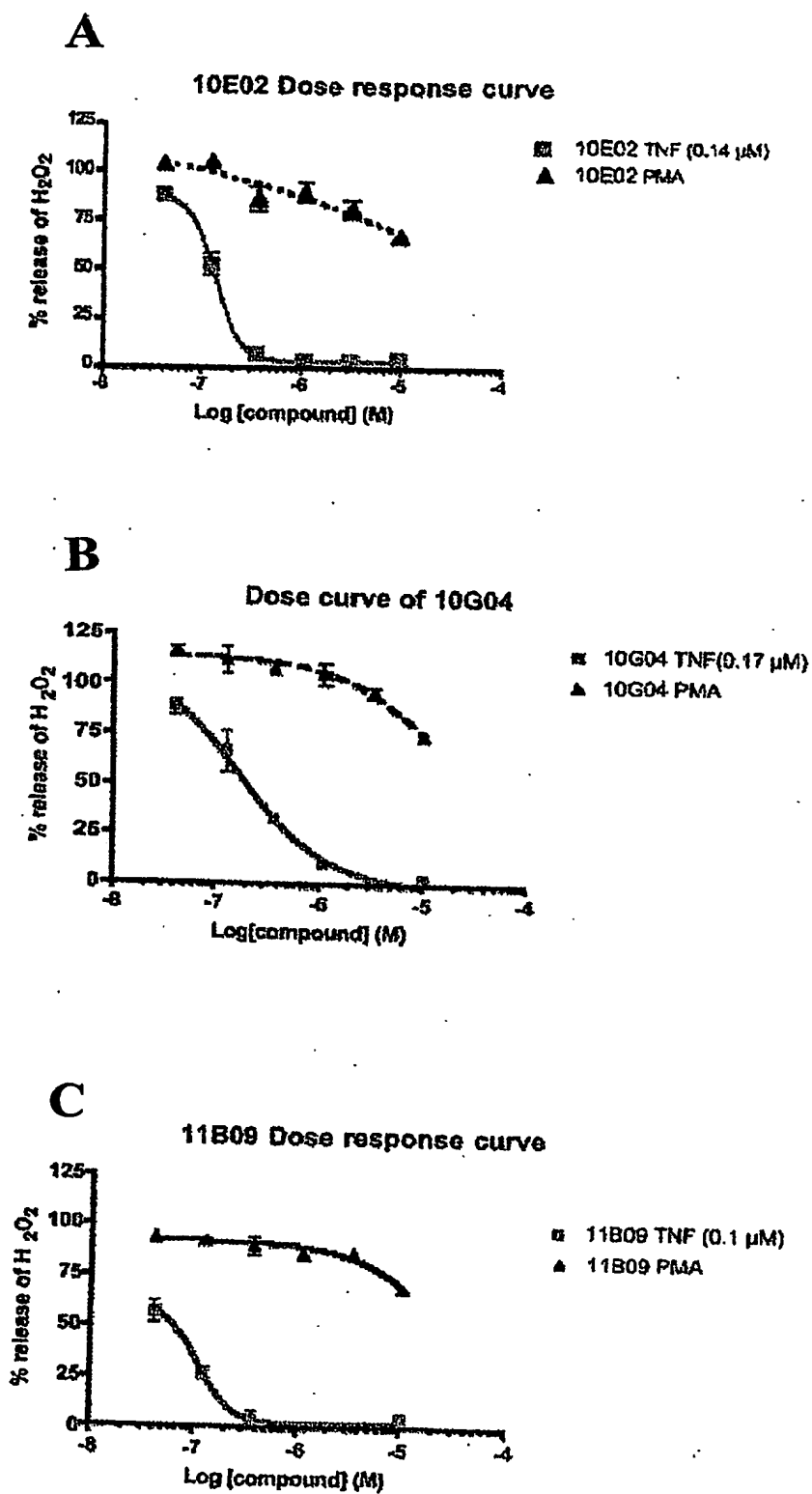


Figure 7

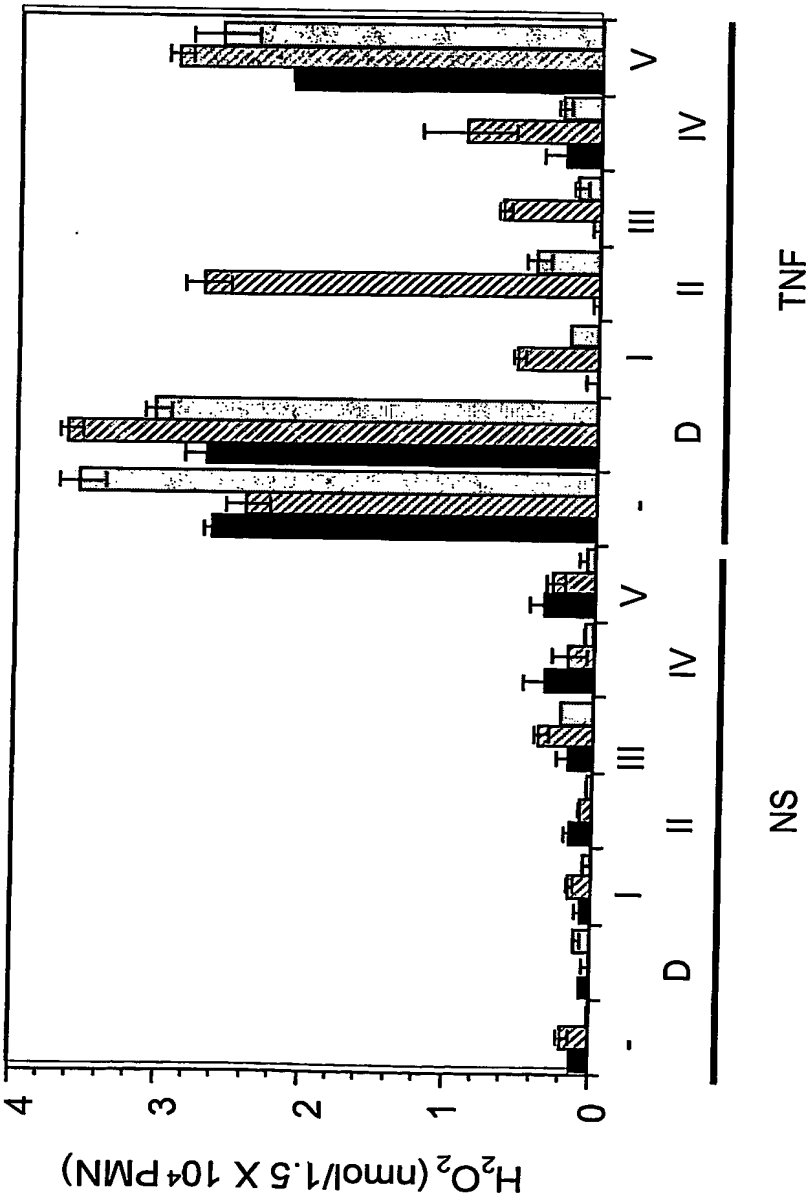
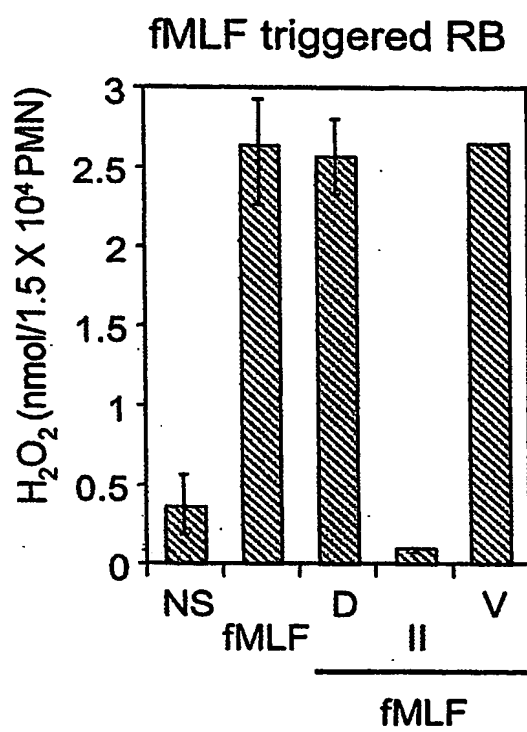


Figure 8

**Figure 9A**

fMLF Triggered RB

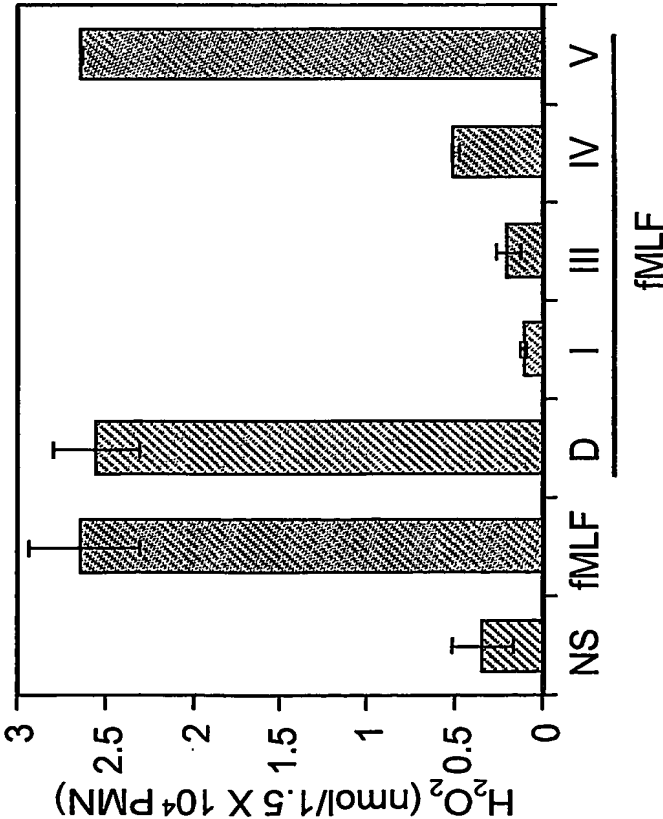


Figure 9 B

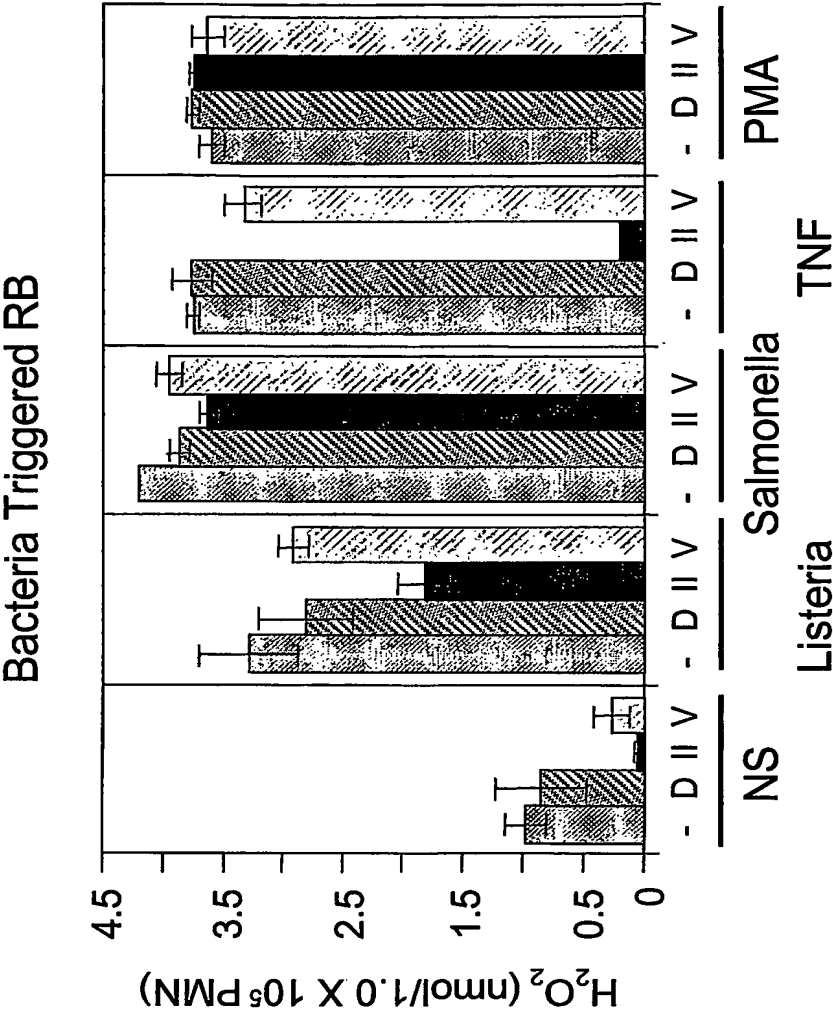


Figure 10A

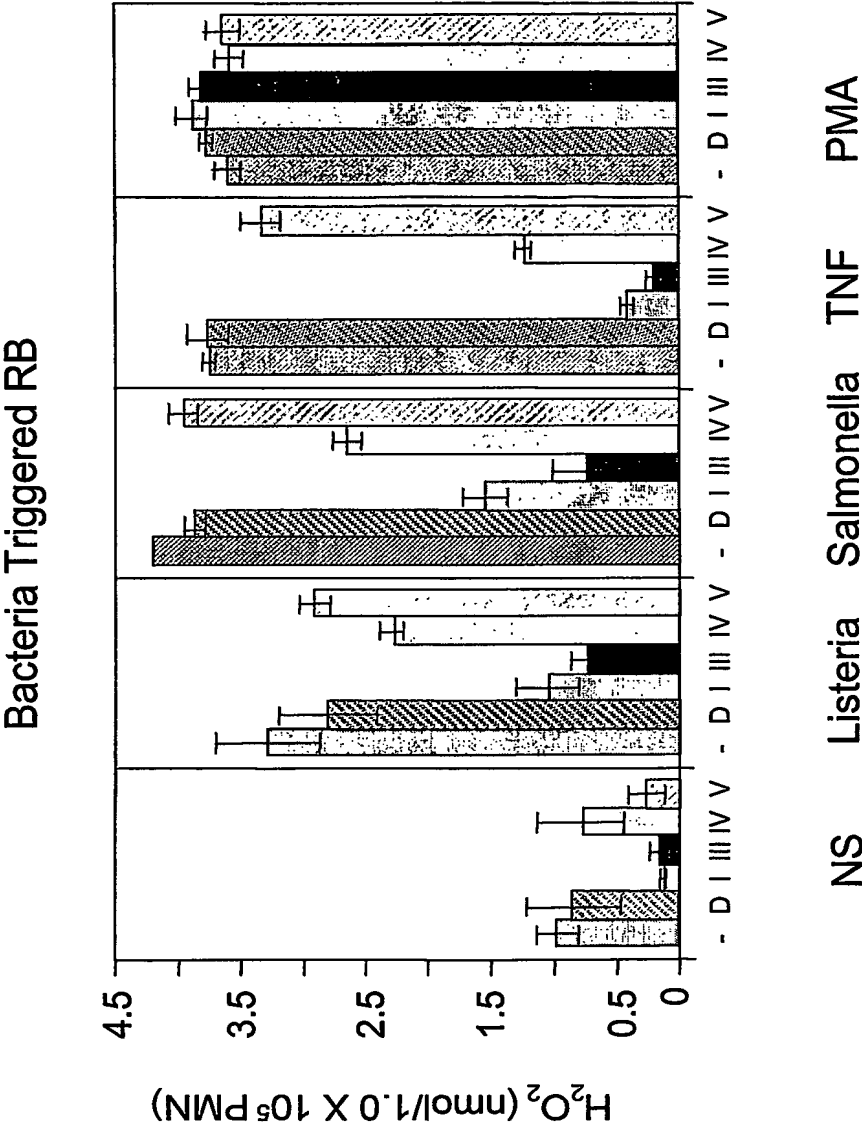
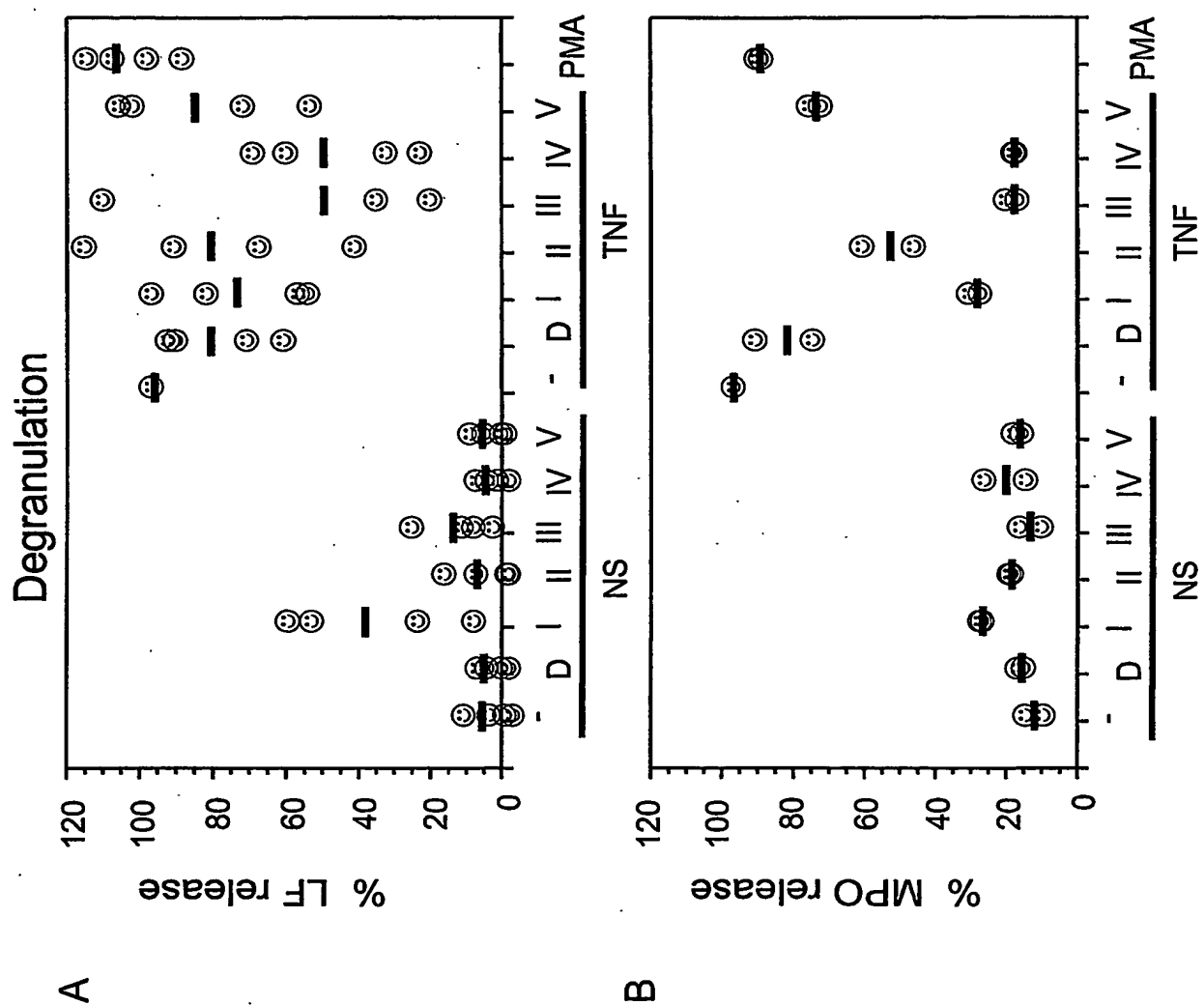


Figure 10B



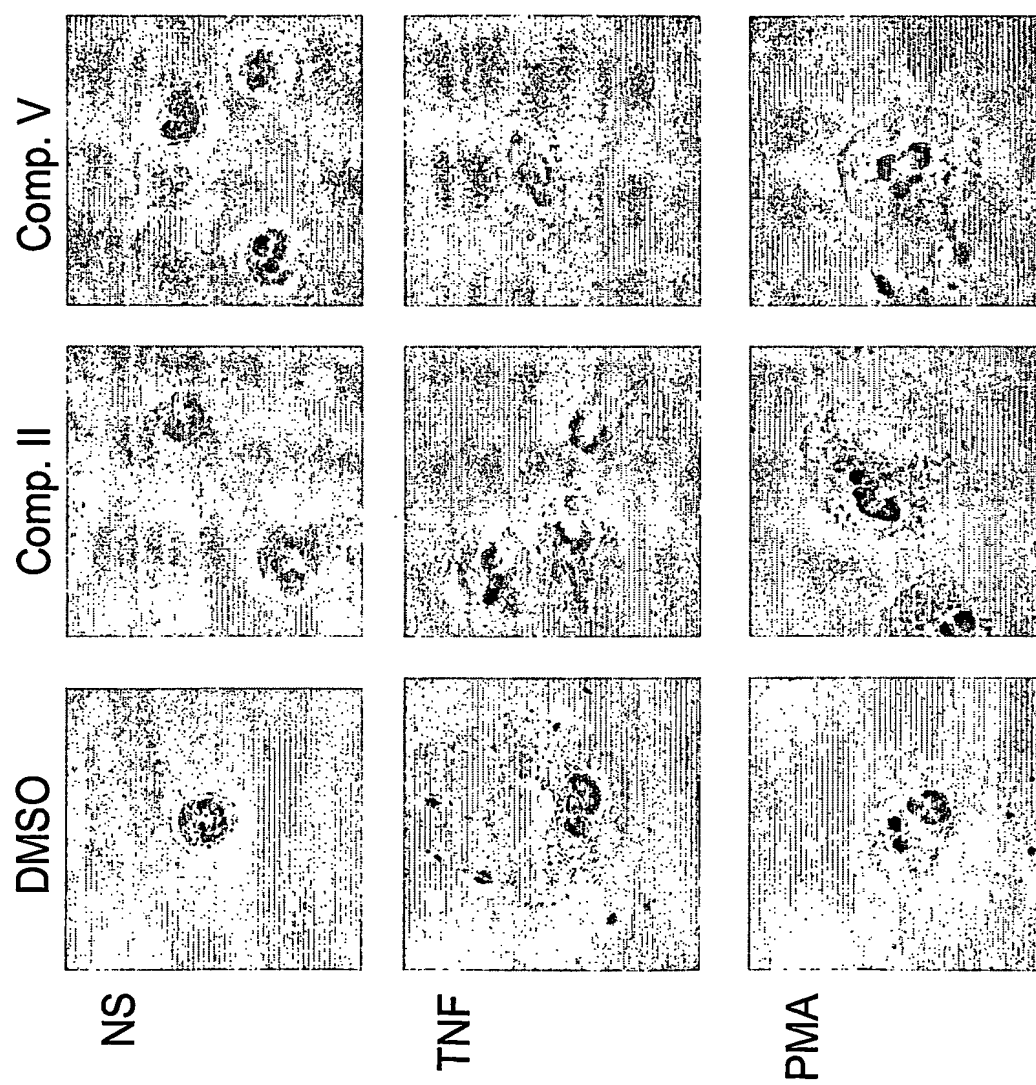


Figure 12A

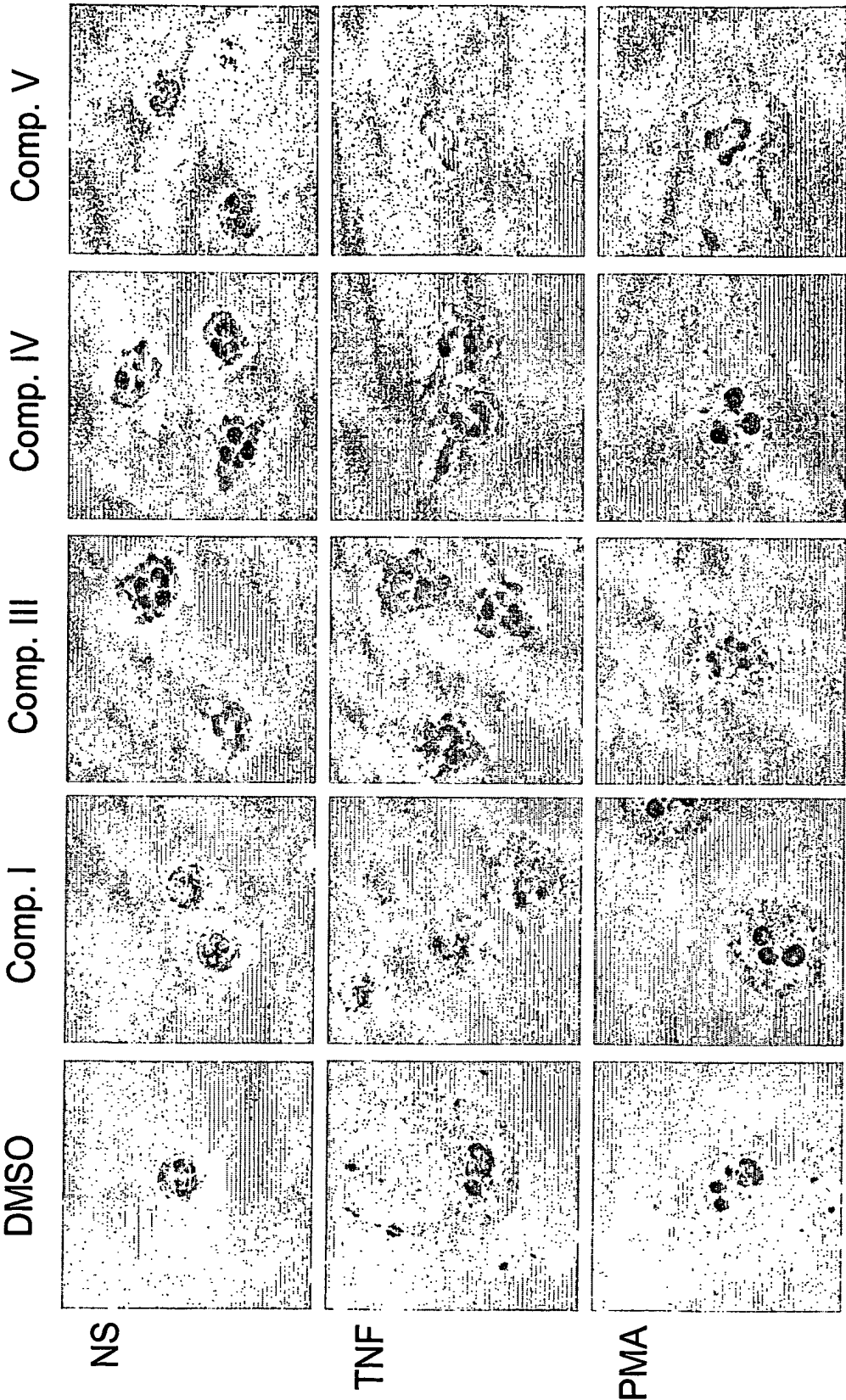


Figure 12B

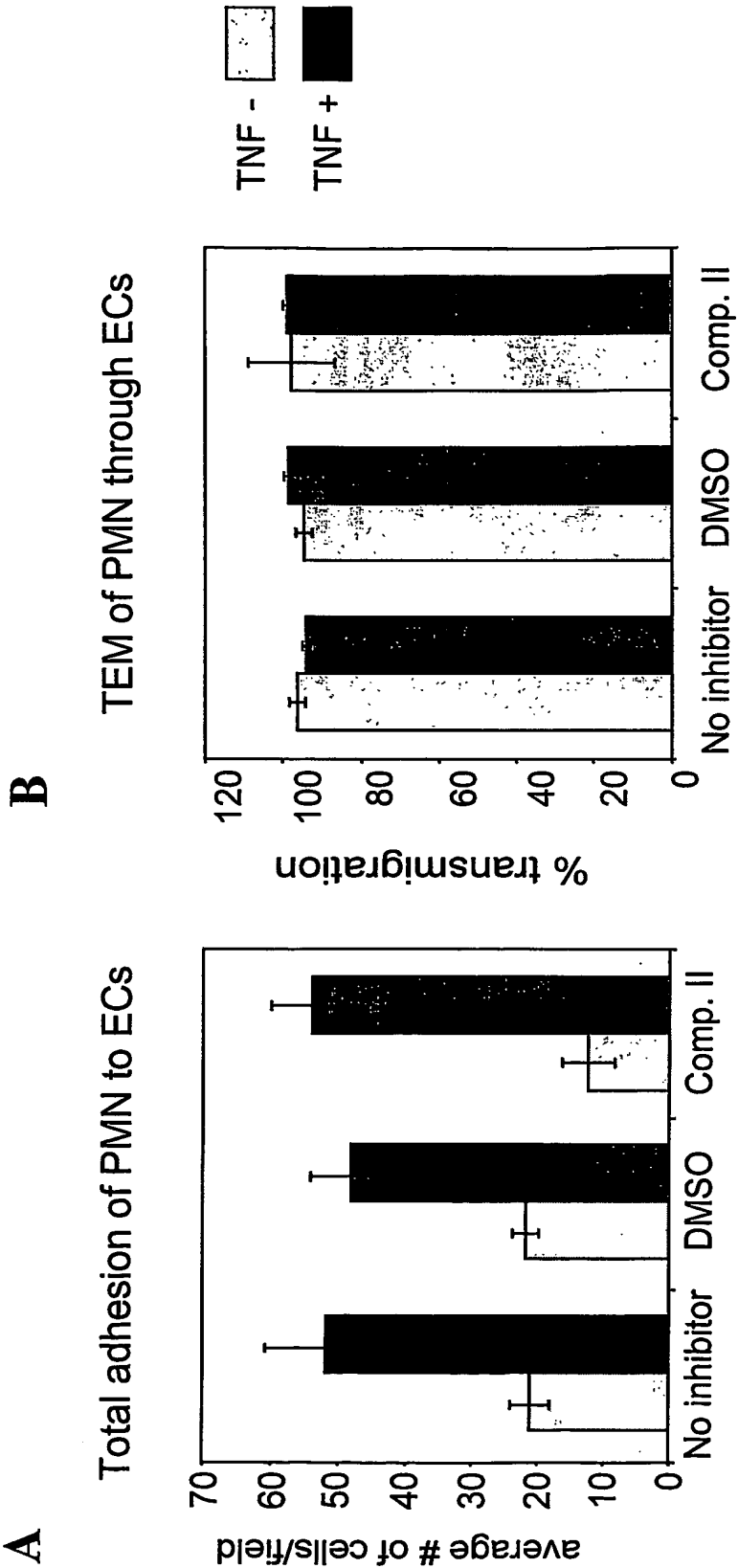


Figure 13

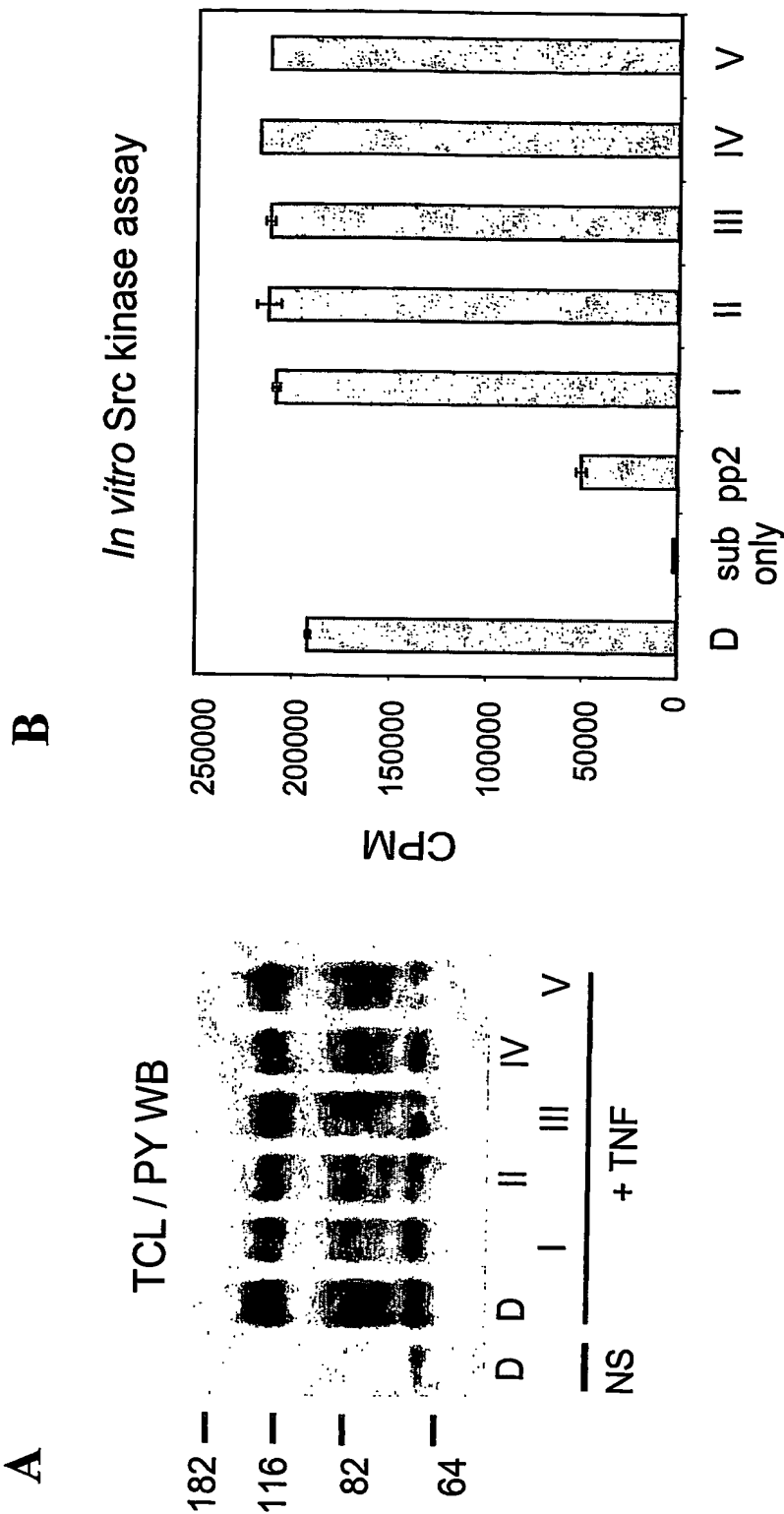


Figure 14A-B

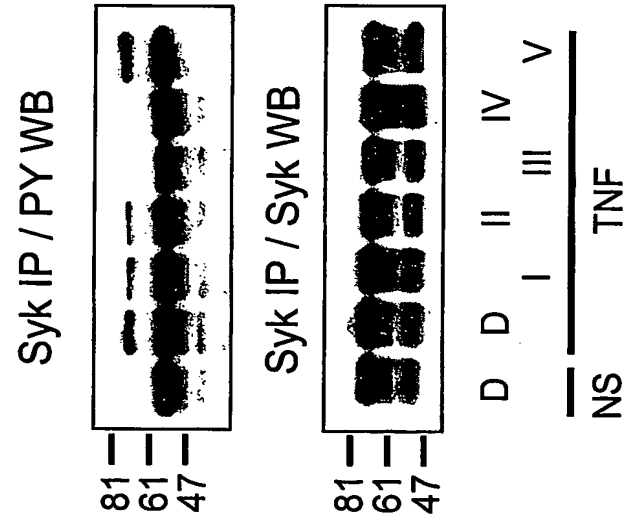


Figure 14C

In vitro Syk Kinase Assay

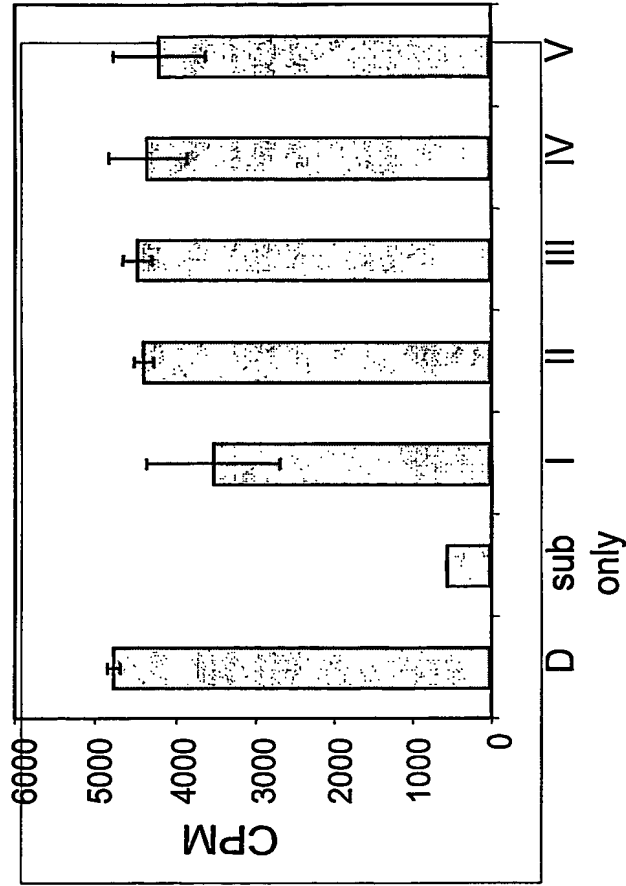


Figure 14D

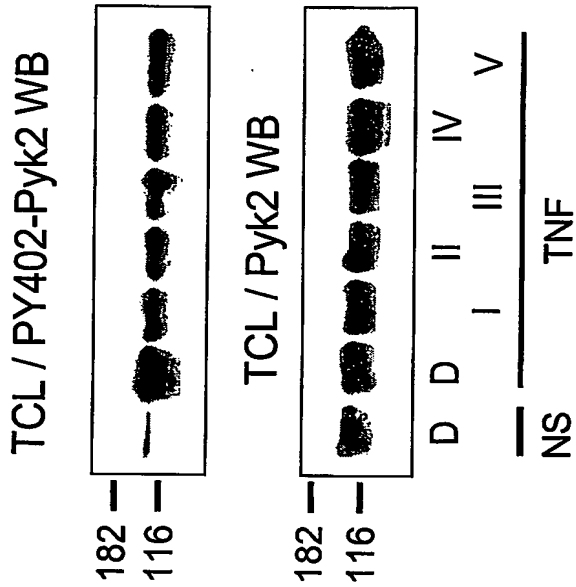


Figure 15

Phagocyte oxidase (phox) (NADPH oxidase)

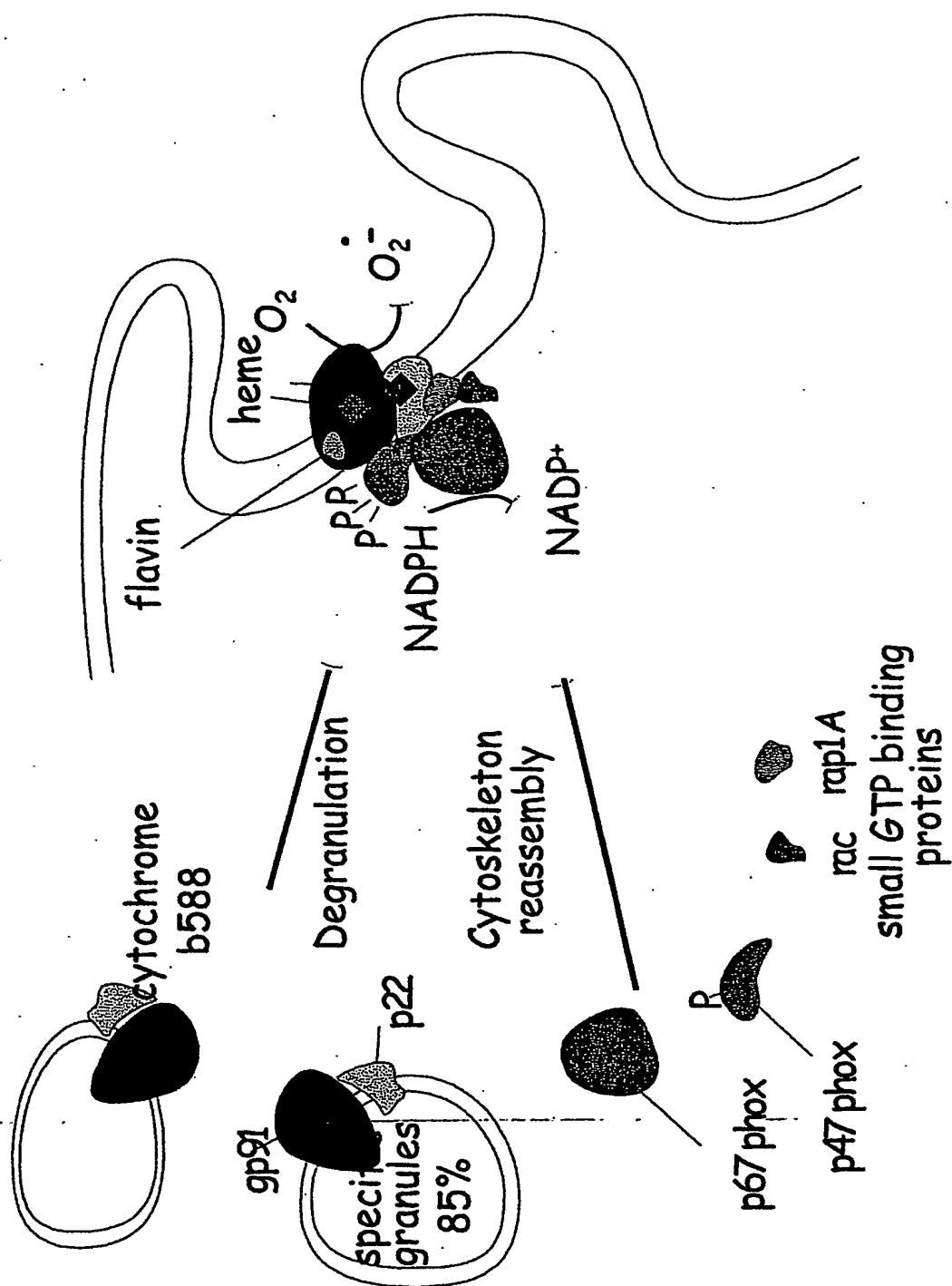
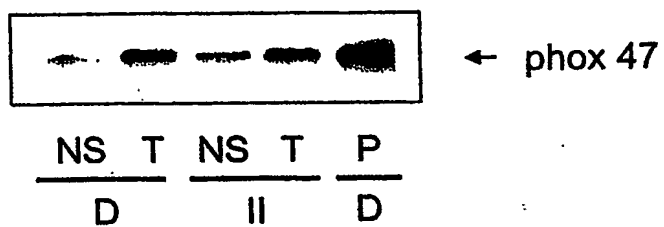


Figure 16

**Figure 17**

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